

Appendix N

UDP/ATC Simulation Modeling Results

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Appendix N-1

**UDP Results for the RC Millimole Regression –Starting One Dose
Lower Than Estimated LD50 - 5000 mg/kg Upper Limit**

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UDP Results for the RC Millimole Regression
Starting One Dose Lower Than Estimated LD50
5000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-4 for chemicals excluded)

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3T3	0.12	Cyto	0.295	7.20	0.91	0.0163	11.2%
		Default	0.255	8.11			
	0.25	Cyto	0.272	8.03	0.93	0.0088	10.4%
		Default	0.250	8.96			
	0.5	Cyto	0.217	8.79	0.97	0.0014	10.0%
		Default	0.208	9.77			
	1.25	Cyto	0.175	9.36	0.98	<.0001	9.4%
		Default	0.167	10.34			
	2	Cyto	0.150	9.43	0.88	<.0001	8.5%
		Default	0.132	10.30			
Average Animal Difference:					0.93		
NHK	0.12	Cyto	0.299	7.33	0.79	0.0232	9.7%
		Default	0.249	8.12			
	0.25	Cyto	0.283	8.14	0.80	0.0185	9.0%
		Default	0.239	8.94			
	0.5	Cyto	0.232	8.93	0.82	0.0024	8.4%
		Default	0.196	9.75			
	1.25	Cyto	0.189	9.47	0.91	<.0001	8.8%
		Default	0.155	10.38			
	2	Cyto	0.168	9.57	0.74	<.0001	7.1%
		Default	0.124	10.31			
Average Animal Difference:					0.81		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals Used	Animals Dead	% Deaths
3T3	0.12	Cyto	23.8%	49.7%	23.7%	2.8%	7.20	3.26	45.3%
		Default	23.3%	51.3%	21.7%	3.6%	8.11	3.43	42.3%
	0.25	Cyto	22.8%	30.0%	41.5%	5.7%	8.03	3.59	44.7%
		Default	22.5%	31.4%	38.6%	7.5%	8.96	3.78	42.2%
	0.5	Cyto	20.2%	18.5%	51.5%	9.8%	8.79	3.95	44.9%
		Default	19.6%	18.9%	48.0%	13.5%	9.77	4.16	42.6%
	1.25	Cyto	14.2%	12.9%	58.6%	14.2%	9.36	4.38	46.8%
		Default	13.2%	13.3%	53.2%	20.3%	10.34	4.62	44.7%
	2	Cyto	11.9%	12.1%	61.6%	14.4%	9.43	4.49	47.6%
		Default	10.4%	12.3%	56.7%	20.5%	10.30	4.73	45.9%
NHK	0.12	Cyto	25.3%	49.1%	22.6%	2.9%	7.33	3.26	44.5%
		Default	25.0%	50.5%	20.9%	3.6%	8.12	3.38	41.7%
	0.25	Cyto	24.3%	29.6%	40.1%	6.0%	8.14	3.58	44.0%
		Default	23.9%	31.1%	37.6%	7.3%	8.94	3.71	41.6%
	0.5	Cyto	21.6%	18.3%	49.5%	10.6%	8.93	3.96	44.3%
		Default	21.1%	18.7%	47.0%	13.2%	9.75	4.10	42.0%
	1.25	Cyto	15.0%	12.8%	57.3%	15.0%	9.47	4.38	46.3%
		Default	13.9%	13.1%	52.4%	20.5%	10.38	4.59	44.2%
	2	Cyto	11.9%	12.0%	60.4%	15.6%	9.57	4.52	47.3%
		Default	10.8%	12.2%	56.2%	20.7%	10.31	4.69	45.6%

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
1	3T3	0.12	Cyto	0.735	9.87	0.78	0.4011	7.3%	
			Default	0.478	10.65				
		0.25	Cyto	0.687	10.42	0.86	0.3538	7.6%	
			Default	0.294	11.28				
		0.5	Cyto	0.639	10.80	0.95	0.1937	8.1%	
			Default	0.158	11.76				
		1.25	Cyto	0.556	11.14	0.94	0.1354	7.8%	
			Default	0.133	12.08				
	2	Cyto	0.473	10.99	0.87	0.1354	7.3%		
		Default	0.122	11.86					
	Average Animal Difference:						0.88		
	NHK	0.12	Cyto	0.540	10.72	-0.09	0.4011	-0.8%	
			Default	0.490	10.63				
		0.25	Cyto	0.542	11.35	-0.29	0.1627	-2.6%	
			Default	0.374	11.06				
		0.5	Cyto	0.501	11.79	-0.25	0.1627	-2.2%	
			Default	0.251	11.54				
		1.25	Cyto	0.453	12.00	-0.03	0.2285	-0.3%	
			Default	0.159	11.97				
	2	Cyto	0.437	11.78	-0.06	0.2670	-0.6%		
	Default	0.136	11.72						
Average Animal Difference:						-0.15			
2	3T3	0.12	Cyto	0.779	8.04	0.004	0.1618	0.05%	
			Default	0.236	8.04				
		0.25	Cyto	0.676	8.66	-0.12	0.1618	-1.3%	
			Default	0.143	8.54				
		0.5	Cyto	0.723	9.15	-0.09	0.3429	-1.0%	
			Default	0.183	9.06				
		1.25	Cyto	0.684	9.67	-0.17	0.3429	-1.8%	
			Default	0.150	9.50				
	2	Cyto	0.538	9.83	-0.20	0.2732	-2.0%		
		Default	0.094	9.64					
	Average Animal Difference:						-0.11		
	NHK	0.12	Cyto	0.362	7.35	0.87	0.0645	10.5%	
			Default	0.307	8.22				
		0.25	Cyto	0.190	8.01	0.78	0.0167	8.8%	
			Default	0.171	8.79				
		0.5	Cyto	0.241	8.48	0.86	0.0331	9.2%	
			Default	0.242	9.34				
		1.25	Cyto	0.196	9.00	0.76	0.0331	7.8%	
			Default	0.212	9.76				
	2	Cyto	0.110	9.30	0.46	0.0464	4.7%		
	Default	0.134	9.76						
Average Animal Difference:						0.74			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
3	3T3	0.12	Cyto	0.261	6.59	0.03	0.3772	0.5%	
			Default	0.351	6.63				
		0.25	Cyto	0.278	6.95	0.01	0.4688	0.2%	
			Default	0.333	6.96				
		0.5	Cyto	0.184	7.61	0.09	0.4073	1.2%	
			Default	0.230	7.70				
		1.25	Cyto	0.081	8.68	0.01	0.4073	0.1%	
			Default	0.101	8.69				
		2	Cyto	0.059	9.12	0.02	0.4073	0.2%	
			Default	0.070	9.14				
	Average Animal Difference:						0.03		
	NHK	0.12	Cyto	0.428	7.02	-0.11	0.4073	-1.5%	
			Default	0.376	6.92				
		0.25	Cyto	0.355	7.26	-0.04	0.5000	-0.6%	
			Default	0.336	7.22				
		0.5	Cyto	0.264	7.88	-0.06	0.4688	-0.7%	
			Default	0.218	7.82				
		1.25	Cyto	0.137	8.77	-0.01	0.4688	-0.1%	
			Default	0.122	8.76				
		2	Cyto	0.094	9.19	-0.03	0.4688	-0.4%	
		Default	0.059	9.16					
Average Animal Difference:						-0.05			
4	3T3	0.12	Cyto	0.203	6.69	0.61	0.1354	8.3%	
			Default	0.349	7.30				
		0.25	Cyto	0.111	7.42	0.65	0.1118	8.1%	
			Default	0.321	8.07				
		0.5	Cyto	0.061	7.91	0.84	0.0746	9.6%	
			Default	0.337	8.76				
		1.25	Cyto	0.057	8.63	0.65	0.0388	7.0%	
			Default	0.216	9.28				
		2	Cyto	0.067	8.97	0.52	0.0094	5.5%	
			Default	0.136	9.49				
	Average Animal Difference:						0.65		
	NHK	0.12	Cyto	0.231	6.71	0.60	0.0917	8.2%	
			Default	0.338	7.31				
		0.25	Cyto	0.124	7.45	0.61	0.0917	7.6%	
			Default	0.313	8.06				
		0.5	Cyto	0.058	7.93	0.81	0.0917	9.3%	
			Default	0.337	8.74				
		1.25	Cyto	0.043	8.66	0.65	0.0193	6.9%	
			Default	0.212	9.31				
		2	Cyto	0.038	9.04	0.42	0.0152	4.4%	
		Default	0.136	9.46					
Average Animal Difference:						0.62			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
5	3T3	0.12	Cyto	0.340	7.81	1.36	0.0121	14.8%	
			Default	0.259	9.16				
		0.25	Cyto	0.285	8.76	1.51	0.0018	14.7%	
			Default	0.149	10.28				
		0.5	Cyto	0.201	9.23	1.52	0.0004	14.1%	
			Default	0.084	10.75				
		1.25	Cyto	0.159	9.24	1.43	0.0004	13.4%	
			Default	0.067	10.68				
		2	Cyto	0.122	9.19	1.18	0.0004	11.4%	
			Default	0.048	10.37				
	Average Animal Difference:						1.40		
	NHK	0.12	Cyto	0.326	7.88	1.25	0.0059	13.7%	
			Default	0.249	9.13				
		0.25	Cyto	0.258	8.79	1.46	0.0011	14.3%	
			Default	0.135	10.26				
		0.5	Cyto	0.196	9.29	1.45	0.0004	13.5%	
			Default	0.078	10.73				
		1.25	Cyto	0.127	9.21	1.49	0.0004	13.9%	
		Default	0.049	10.69					
	2	Cyto	0.094	9.20	1.13	0.0004	11.0%		
		Default	0.048	10.33					
Average Animal Difference:						1.36			
6	3T3	0.12	Cyto	0.450	4.99	1.70	0.0032	25.4%	
			Default	0.370	6.69				
		0.25	Cyto	0.523	6.30	1.62	0.0257	20.4%	
			Default	0.437	7.92				
		0.5	Cyto	0.394	8.05	1.54	0.0102	16.1%	
			Default	0.271	9.59				
		1.25	Cyto	0.293	9.03	1.88	0.0007	17.3%	
			Default	0.057	10.91				
		2	Cyto	0.263	8.92	1.84	0.0007	17.1%	
			Default	0.035	10.75				
	Average Animal Difference:						1.72		
	NHK	0.12	Cyto	0.439	5.19	1.45	0.0183	21.8%	
			Default	0.345	6.64				
		0.25	Cyto	0.530	6.40	1.42	0.0729	18.2%	
			Default	0.433	7.83				
		0.5	Cyto	0.405	8.17	1.35	0.0239	14.2%	
			Default	0.279	9.52				
		1.25	Cyto	0.306	9.24	1.66	0.0006	15.3%	
		Default	0.042	10.90					
	2	Cyto	0.312	9.20	1.60	0.0011	14.8%		
		Default	0.032	10.80					
Average Animal Difference:						1.50			

Notes:

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at Numbers are numbers of animals unless otherwise specified

Sigma - reciprocal of slope

Cyto= using NRU-determined starting dose

Default - using default starting dose of 175 mg/kg

Appendix N-2

**UDP Results for the RC Rat-Only Weight Regression –Starting One
Dose Lower Than Estimated LD50 - 5000 mg/kg Upper Limit**

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**UDP Results for the RC Rat-Only Weight Regression
Starting One Dose Lower Than Estimated LD50
5000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-5 for chemicals excluded).**

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3T3	0.12	Cyto	0.292	7.11	1.03	0.0075	12.7%
		Default	0.254	8.14			
	0.25	Cyto	0.269	7.91	1.08	0.0042	12.0%
		Default	0.249	8.98			
	0.5	Cyto	0.215	8.66	1.13	0.0003	11.6%
		Default	0.207	9.79			
	1.25	Cyto	0.175	9.26	1.09	<.0001	10.6%
		Default	0.166	10.36			
2	Cyto	0.150	9.36	0.95	<.0001	9.2%	
	Default	0.132	10.31				
Average Animal Difference:					1.06		

NHK	0.12	Cyto	0.297	7.25	0.88	0.0158	10.9%
		Default	0.249	8.13			
	0.25	Cyto	0.278	8.03	0.92	0.0093	10.3%
		Default	0.240	8.96			
	0.5	Cyto	0.226	8.83	0.94	0.0012	9.6%
		Default	0.197	9.77			
	1.25	Cyto	0.186	9.40	0.99	<.0001	9.5%
		Default	0.155	10.39			
2	Cyto	0.166	9.50	0.81	<.0001	7.9%	
	Default	0.123	10.32				
Average Animal Difference:					0.91		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals Used	Animals Dead	% Deaths
3T3	0.12	Cyto	23.8%	49.5%	24.1%	2.7%	7.11	3.24	45.6%
		Default	23.3%	51.6%	21.5%	3.6%	8.14	3.44	42.3%
	0.25	Cyto	22.9%	29.8%	41.9%	5.4%	7.91	3.56	45.0%
		Default	22.5%	31.7%	38.3%	7.5%	8.98	3.79	42.2%
	0.5	Cyto	20.2%	18.4%	52.1%	9.2%	8.66	3.91	45.2%
		Default	19.6%	19.1%	47.7%	13.6%	9.79	4.18	42.6%
	1.25	Cyto	14.3%	13.0%	59.4%	13.4%	9.26	4.35	47.0%
		Default	13.3%	13.3%	53.0%	20.5%	10.36	4.63	44.7%
2	Cyto	12.0%	12.1%	61.9%	14.0%	9.36	4.47	47.8%	
	Default	10.4%	12.3%	56.7%	20.6%	10.31	4.73	45.9%	
NHK	0.12	Cyto	25.3%	49.2%	22.7%	2.8%	7.25	3.24	44.7%
		Default	25.0%	50.5%	20.9%	3.6%	8.13	3.39	41.7%
	0.25	Cyto	24.3%	29.5%	40.6%	5.5%	8.03	3.56	44.3%
		Default	24.0%	31.2%	37.5%	7.3%	8.96	3.72	41.6%
	0.5	Cyto	21.6%	18.3%	50.2%	9.9%	8.83	3.93	44.5%
		Default	21.1%	18.8%	46.9%	13.3%	9.77	4.11	42.0%
	1.25	Cyto	15.0%	12.8%	57.8%	14.5%	9.40	4.37	46.4%
		Default	13.9%	13.2%	52.4%	20.6%	10.39	4.60	44.3%
2	Cyto	12.1%	12.1%	60.8%	15.1%	9.50	4.50	47.4%	
	Default	10.8%	12.2%	56.2%	20.8%	10.32	4.70	45.6%	

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
1	3T3	0.12	Cyto	0.711	9.93	0.73	0.3538	6.8%	
			Default	0.478	10.66				
		0.25	Cyto	0.665	10.47	0.80	0.3538	7.1%	
			Default	0.297	11.27				
		0.5	Cyto	0.610	10.85	0.89	0.2285	7.6%	
			Default	0.159	11.75				
		1.25	Cyto	0.528	11.21	0.85	0.1354	7.1%	
			Default	0.124	12.06				
		2	Cyto	0.444	11.05	0.80	0.1627	6.8%	
			Default	0.125	11.85				
	Average Animal Difference:						0.81		
	NHK	0.12	Cyto	0.529	10.59	0.07	0.5000	0.6%	
			Default	0.478	10.66				
		0.25	Cyto	0.490	11.20	-0.09	0.1937	-0.8%	
			Default	0.339	11.12				
		0.5	Cyto	0.437	11.66	-0.08	0.2285	-0.7%	
			Default	0.228	11.58				
		1.25	Cyto	0.400	11.92	0.05	0.2285	0.4%	
			Default	0.153	11.97				
		2	Cyto	0.391	11.71	0.00	0.2670	0.0%	
		Default	0.139	11.71					
Average Animal Difference:						-0.01			
2	3T3	0.12	Cyto	0.591	7.76	0.36	0.1618	4.47%	
			Default	0.268	8.12				
		0.25	Cyto	0.472	8.32	0.30	0.0888	3.5%	
			Default	0.140	8.62				
		0.5	Cyto	0.535	8.80	0.34	0.0888	3.7%	
			Default	0.169	9.14				
		1.25	Cyto	0.482	9.32	0.24	0.0888	2.5%	
			Default	0.141	9.56				
		2	Cyto	0.361	9.60	0.05	0.0888	0.6%	
			Default	0.087	9.66				
	Average Animal Difference:						0.26		
	NHK	0.12	Cyto	0.375	7.36	0.84	0.1208	10.3%	
			Default	0.311	8.20				
		0.25	Cyto	0.222	7.96	0.82	0.0167	9.3%	
			Default	0.185	8.78				
		0.5	Cyto	0.266	8.39	0.94	0.0645	10.1%	
			Default	0.264	9.33				
		1.25	Cyto	0.204	8.92	0.85	0.0236	8.7%	
			Default	0.206	9.77				
		2	Cyto	0.111	9.25	0.53	0.0331	5.4%	
		Default	0.130	9.78					
Average Animal Difference:						0.80			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
3	3T3	0.12	Cyto	0.226	6.66	0.05	0.5000	0.8%	
			Default	0.324	6.71				
		0.25	Cyto	0.185	6.98	0.04	0.5000	0.5%	
			Default	0.294	7.02				
		0.5	Cyto	0.101	7.60	0.15	0.4073	1.9%	
			Default	0.216	7.75				
		1.25	Cyto	0.056	8.66	0.01	0.4688	0.2%	
			Default	0.096	8.67				
		2	Cyto	0.027	9.13	0.01	0.4688	0.1%	
			Default	0.077	9.14				
	Average Animal Difference:						0.05		
	NHK	0.12	Cyto	0.410	7.09	-0.15	0.4377	-2.2%	
			Default	0.370	6.94				
		0.25	Cyto	0.340	7.34	-0.09	0.4688	-1.2%	
			Default	0.326	7.26				
		0.5	Cyto	0.254	7.93	-0.09	0.4073	-1.1%	
			Default	0.211	7.84				
		1.25	Cyto	0.130	8.81	-0.05	0.4073	-0.5%	
			Default	0.124	8.77				
		2	Cyto	0.095	9.21	-0.04	0.4688	-0.5%	
		Default	0.059	9.17					
Average Animal Difference:						-0.08			
4	3T3	0.12	Cyto	0.211	6.68	0.61	0.1118	8.4%	
			Default	0.349	7.29				
		0.25	Cyto	0.124	7.40	0.65	0.1118	8.1%	
			Default	0.323	8.05				
		0.5	Cyto	0.074	7.89	0.86	0.0485	9.8%	
			Default	0.330	8.75				
		1.25	Cyto	0.059	8.64	0.64	0.0309	6.9%	
			Default	0.206	9.28				
		2	Cyto	0.058	8.97	0.51	0.0120	5.4%	
			Default	0.139	9.48				
	Average Animal Difference:						0.65		
	NHK	0.12	Cyto	0.234	6.71	0.60	0.1118	8.2%	
			Default	0.339	7.31				
		0.25	Cyto	0.129	7.43	0.63	0.1118	7.8%	
			Default	0.313	8.06				
		0.5	Cyto	0.064	7.92	0.82	0.0917	9.3%	
			Default	0.335	8.74				
		1.25	Cyto	0.047	8.66	0.65	0.0152	6.9%	
			Default	0.211	9.31				
		2	Cyto	0.041	9.04	0.43	0.0120	4.6%	
		Default	0.133	9.47					
Average Animal Difference:						0.62			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
5	3T3	0.12	Cyto	0.415	7.48	1.70	0.0105	18.5%	
			Default	0.258	9.18				
		0.25	Cyto	0.368	8.42	1.91	0.0015	18.5%	
			Default	0.143	10.33				
		0.5	Cyto	0.280	8.90	1.91	0.0004	17.7%	
			Default	0.082	10.81				
		1.25	Cyto	0.215	9.01	1.71	0.0004	15.9%	
			Default	0.070	10.72				
		2	Cyto	0.169	9.02	1.37	0.0004	13.2%	
			Default	0.055	10.40				
	Average Animal Difference:						1.72		
	NHK	0.12	Cyto	0.371	7.64	1.50	0.0059	16.4%	
			Default	0.248	9.14				
		0.25	Cyto	0.310	8.55	1.75	0.0010	17.0%	
			Default	0.124	10.30				
		0.5	Cyto	0.241	9.07	1.70	0.0004	15.8%	
			Default	0.070	10.77				
		1.25	Cyto	0.150	9.07	1.65	0.0004	15.4%	
			Default	0.045	10.72				
		2	Cyto	0.109	9.07	1.29	0.0004	12.4%	
		Default	0.051	10.35					
Average Animal Difference:						1.58			
6	3T3	0.12	Cyto	0.446	4.96	1.73	0.0086	25.9%	
			Default	0.371	6.69				
		0.25	Cyto	0.534	6.26	1.66	0.0458	21.0%	
			Default	0.438	7.92				
		0.5	Cyto	0.404	7.96	1.63	0.0102	17.0%	
			Default	0.274	9.59				
		1.25	Cyto	0.303	8.93	1.98	0.0007	18.2%	
			Default	0.060	10.92				
		2	Cyto	0.274	8.85	1.89	0.0007	17.6%	
			Default	0.035	10.74				
	Average Animal Difference:						1.78		
	NHK	0.12	Cyto	0.424	5.09	1.55	0.0159	23.3%	
			Default	0.345	6.64				
		0.25	Cyto	0.519	6.30	1.52	0.0578	19.4%	
			Default	0.432	7.82				
		0.5	Cyto	0.404	8.07	1.45	0.0209	15.2%	
			Default	0.280	9.52				
		1.25	Cyto	0.316	9.15	1.76	0.0004	16.1%	
			Default	0.042	10.90				
		2	Cyto	0.315	9.11	1.69	0.0008	15.7%	
		Default	0.031	10.80					
Average Animal Difference:						1.59			

Notes:

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.

Numbers are numbers of animals unless otherwise specified

Sigma - reciprocal of slope

Cyto= using NRU-determined starting dose

Default - using default starting dose of 175 mg/kg

Appendix N-3

**UDP Results for the RC Rat-Only Weight Regression Excluding
Chemicals with Specific Mechanisms of Toxicity - Starting One Dose
Lower Than Estimated LD50 –5000 mg/kg Upper Limit**

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UDP Results for the RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity

Starting One Dose Lower Than Estimated LD50

5000 mg/kg Upper Limit

Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU

(see notes to Table 6-5 for chemicals excluded).

Summary of Animals Used by Cell Type

Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings
3T3	0.12	Cyto	0.311	7.08	1.08	0.0052	13.3%
		Default	0.249	8.16			
	0.25	Cyto	0.283	7.87	1.14	0.0022	12.7%
		Default	0.244	9.01			
	0.5	Cyto	0.227	8.64	1.16	0.0002	11.8%
		Default	0.203	9.80			
	1.25	Cyto	0.190	9.21	1.15	<.0001	11.1%
		Default	0.164	10.36			
	2	Cyto	0.168	9.33	0.97	<.0001	9.4%
		Default	0.131	10.30			
Average Animal Difference:					1.10		

NHK	0.12	Cyto	0.317	7.15	1.00	0.0093	12.2%
		Default	0.247	8.15			
	0.25	Cyto	0.295	7.93	1.04	0.0045	11.6%
		Default	0.238	8.97			
	0.5	Cyto	0.241	8.73	1.05	0.0005	10.7%
		Default	0.197	9.78			
	1.25	Cyto	0.198	9.29	1.10	<.0001	10.6%
		Default	0.156	10.39			
	2	Cyto	0.178	9.41	0.90	<.0001	8.7%
		Default	0.124	10.31			
Average Animal Difference:					1.02		

Summary of Animal Deaths by Cell Type

Cell Type	Sigma	Method	3 Animals at Limit Dose	5 Reversals	Likelihood Ratio	Max Animals	Animals	Died	% Dead
3T3	0.12	Cyto	23.8%	49.4%	24.1%	2.7%	7.08	3.34	47.24%
		Default	23.3%	51.8%	21.3%	3.6%	8.16	3.45	42.34%
	0.25	Cyto	22.9%	29.7%	42.0%	5.3%	7.87	3.66	46.53%
		Default	22.5%	32.0%	38.0%	7.5%	9.01	3.81	42.23%
	0.5	Cyto	20.3%	18.2%	52.4%	9.2%	8.64	4.03	46.59%
		Default	19.7%	19.1%	47.7%	13.6%	9.80	4.18	42.69%
	1.25	Cyto	14.5%	12.9%	59.4%	13.3%	9.21	4.44	48.18%
		Default	13.3%	13.3%	52.9%	20.5%	10.36	4.63	44.70%
	2	Cyto	12.4%	12.0%	61.6%	14.0%	9.33	4.55	48.79%
		Default	10.4%	12.3%	56.8%	20.5%	10.30	4.73	45.91%
NHK	0.12	Cyto	25.3%	48.9%	22.9%	2.8%	7.15	3.29	46.07%
		Default	25.0%	50.8%	20.6%	3.6%	8.15	3.40	41.70%
	0.25	Cyto	24.3%	29.5%	40.8%	5.4%	7.93	3.61	45.55%
		Default	24.0%	31.5%	37.2%	7.4%	8.97	3.73	41.63%
	0.5	Cyto	21.7%	18.1%	50.5%	9.7%	8.73	3.99	45.75%
		Default	21.1%	18.9%	46.8%	13.3%	9.78	4.12	42.09%
	1.25	Cyto	15.3%	12.7%	58.1%	13.9%	9.29	4.41	47.51%
		Default	14.0%	13.2%	52.4%	20.5%	10.39	4.60	44.28%
	2	Cyto	12.5%	12.1%	60.7%	14.8%	9.41	4.55	48.30%
		Default	10.8%	12.3%	56.1%	20.8%	10.31	4.70	45.57%

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
1	3T3	0.12	Cyto	0.668	10.31	0.31	0.4011	2.9%	
		0.12	Default	0.475	10.62				
		0.25	Cyto	0.618	10.86	0.36	0.5000	3.2%	
		0.25	Default	0.303	11.22				
		0.5	Cyto	0.554	11.26	0.42	0.4501	3.6%	
		0.5	Default	0.171	11.68				
		1.25	Cyto	0.499	11.58	0.44	0.4011	3.6%	
		1.25	Default	0.123	12.02				
	2	Cyto	0.438	11.39	0.40	0.4011	3.4%		
	2	Default	0.129	11.78					
	Average Animal Difference:						0.39		
	NHK	0.12	Cyto	0.446	10.83	-0.18	0.5000	-1.6%	
		0.12	Default	0.478	10.66				
		0.25	Cyto	0.384	11.44	-0.34	0.1937	-3.0%	
		0.25	Default	0.347	11.10				
		0.5	Cyto	0.319	11.90	-0.35	0.0917	-3.0%	
		0.5	Default	0.227	11.55				
		1.25	Cyto	0.300	12.14	-0.18	0.1011	-1.5%	
		1.25	Default	0.155	11.95				
		2	Cyto	0.292	11.95	-0.25	0.0917	-2.1%	
2		Default	0.133	11.70					
Average Animal Difference:						-0.26			
2	3T3	0.12	Cyto	0.594	7.92	0.15	0.1618	1.9%	
		0.12	Default	0.249	8.07				
		0.25	Cyto	0.485	8.51	0.07	0.2732	0.9%	
		0.25	Default	0.130	8.58				
		0.5	Cyto	0.548	9.03	0.02	0.4196	0.3%	
		0.5	Default	0.130	9.05				
		1.25	Cyto	0.490	9.51	-0.03	0.3429	-0.3%	
		1.25	Default	0.113	9.49				
	2	Cyto	0.372	9.77	-0.14	0.5000	-1.4%		
	2	Default	0.086	9.63					
	Average Animal Difference:						0.02		
	NHK	0.12	Cyto	0.364	7.30	0.89	0.0645	10.9%	
		0.12	Default	0.317	8.19				
		0.25	Cyto	0.217	7.88	0.86	0.0464	9.9%	
		0.25	Default	0.189	8.74				
		0.5	Cyto	0.278	8.30	0.98	0.0464	10.6%	
		0.5	Default	0.253	9.28				
		1.25	Cyto	0.222	8.81	0.93	0.0331	9.6%	
		1.25	Default	0.195	9.74				
		2	Cyto	0.149	9.21	0.54	0.0464	5.5%	
2		Default	0.120	9.75					
Average Animal Difference:						0.84			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
3	3T3	0.12	Cyto	0.289	6.99	-0.06	0.4688	-0.9%	
		0.12	Default	0.306	6.93				
		0.25	Cyto	0.218	7.30	-0.08	0.4688	-1.1%	
		0.25	Default	0.251	7.22				
		0.5	Cyto	0.150	7.84	-0.02	0.4688	-0.2%	
		0.5	Default	0.183	7.82				
		1.25	Cyto	0.105	8.74	-0.04	0.4688	-0.4%	
		1.25	Default	0.098	8.70				
	2	Cyto	0.055	9.21	-0.12	0.1004	-1.3%		
	2	Default	0.082	9.09					
	Average Animal Difference:						-0.06		
	NHK	0.12	Cyto	0.398	7.26	-0.19	0.3483	-2.6%	
		0.12	Default	0.343	7.08				
		0.25	Cyto	0.312	7.49	-0.12	0.5000	-1.6%	
		0.25	Default	0.285	7.37				
		0.5	Cyto	0.243	8.03	-0.16	0.4073	-2.0%	
		0.5	Default	0.195	7.87				
		1.25	Cyto	0.123	8.85	-0.13	0.2932	-1.4%	
		1.25	Default	0.129	8.72				
	2	Cyto	0.078	9.21	-0.08	0.2431	-0.9%		
2	Default	0.068	9.13						
Average Animal Difference:						-0.13			
4	3T3	0.12	Cyto	0.175	6.58	0.73	0.0917	10.0%	
		0.12	Default	0.366	7.31				
		0.25	Cyto	0.122	7.31	0.78	0.0917	9.6%	
		0.25	Default	0.336	8.08				
		0.5	Cyto	0.056	7.81	1.00	0.0245	11.4%	
		0.5	Default	0.352	8.81				
		1.25	Cyto	0.038	8.58	0.75	0.0120	8.0%	
		1.25	Default	0.213	9.32				
	2	Cyto	0.064	8.94	0.55	0.0120	5.8%		
	2	Default	0.139	9.49					
	Average Animal Difference:						0.76		
	NHK	0.12	Cyto	0.222	6.61	0.69	0.0917	9.5%	
		0.12	Default	0.341	7.31				
		0.25	Cyto	0.140	7.33	0.71	0.0746	8.9%	
		0.25	Default	0.320	8.04				
		0.5	Cyto	0.061	7.86	0.90	0.0309	10.3%	
		0.5	Default	0.333	8.76				
		1.25	Cyto	0.036	8.59	0.74	0.0074	7.9%	
		1.25	Default	0.201	9.34				
	2	Cyto	0.038	9.00	0.49	0.0120	5.1%		
2	Default	0.130	9.48						
Average Animal Difference:						0.71			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Toxcat	Cell	Sigma	Method	Std. Error	Animals	Difference	P-Value*	% Savings	
5	3T3	0.12	Cyto	0.369	7.19	2.00	0.0038	21.8%	
		0.12	Default	0.259	9.18				
		0.25	Cyto	0.326	8.07	2.31	0.0004	22.2%	
		0.25	Default	0.129	10.38				
		0.5	Cyto	0.234	8.62	2.22	0.0004	20.5%	
		0.5	Default	0.071	10.84				
		1.25	Cyto	0.153	8.76	2.01	0.0004	18.7%	
		1.25	Default	0.054	10.77				
	2	Cyto	0.116	8.81	1.60	0.0004	15.3%		
	2	Default	0.054	10.41					
	Average Animal Difference:						2.03		
	NHK	0.12	Cyto	0.393	7.41	1.75	0.0051	19.1%	
		0.12	Default	0.248	9.15				
		0.25	Cyto	0.325	8.28	2.05	0.0008	19.9%	
		0.25	Default	0.126	10.33				
		0.5	Cyto	0.260	8.84	1.98	0.0004	18.3%	
		0.5	Default	0.073	10.82				
		1.25	Cyto	0.173	8.90	1.83	0.0004	17.1%	
		1.25	Default	0.047	10.73				
	2	Cyto	0.139	8.92	1.44	0.0004	13.9%		
2	Default	0.052	10.36						
Average Animal Difference:						1.81			
6	3T3	0.12	Cyto	0.462	4.68	2.01	0.0062	30.1%	
		0.12	Default	0.371	6.69				
		0.25	Cyto	0.544	6.00	1.92	0.0221	24.3%	
		0.25	Default	0.438	7.92				
		0.5	Cyto	0.400	7.71	1.88	0.0038	19.6%	
		0.5	Default	0.274	9.59				
		1.25	Cyto	0.281	8.63	2.29	0.0007	21.0%	
		1.25	Default	0.060	10.93				
	2	Cyto	0.249	8.59	2.16	0.0007	20.1%		
	2	Default	0.037	10.75					
	Average Animal Difference:						2.05		
	NHK	0.12	Cyto	0.439	4.76	1.88	0.0051	28.4%	
		0.12	Default	0.345	6.64				
		0.25	Cyto	0.543	5.98	1.84	0.0209	23.5%	
		0.25	Default	0.432	7.82				
		0.5	Cyto	0.426	7.75	1.77	0.0059	18.6%	
		0.5	Default	0.281	9.52				
		1.25	Cyto	0.281	8.76	2.15	0.0004	19.7%	
		1.25	Default	0.042	10.91				
	2	Cyto	0.272	8.77	2.04	0.0004	18.9%		
2	Default	0.029	10.81						
Average Animal Difference:						1.94			

Notes:

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.

Numbers are numbers of animals unless otherwise specified

Sigma - reciprocal of slope

Cyto= using NRU-determined starting dose

Default - using default starting dose of 175 mg/kg

Appendix N-4

ATC Results for the RC Millimole Regression - 2000 mg/kg Upper Limit

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ATC Results for the RC Millimole Regression
2000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-4 for chemicals excluded)

Summary of Animals Used and Deaths by Cell Type

Cell Type	Sigma	Method	No. Animals Dead	% Deaths	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings
NHK	0.12	Cyto	2.34	24.4%	0.340	9.57	1.27	0.0018	11.7%
		Default	2.97	27.4%	0.208	10.84			
	0.25	Cyto	2.49	25.9%	0.322	9.61	1.26	0.0075	11.6%
		Default	3.14	28.9%	0.189	10.87			
	0.5	Cyto	2.82	29.0%	0.299	9.72	1.21	0.0003	11.1%
		Default	3.47	31.8%	0.155	10.93			
	1.25	Cyto	3.55	35.9%	0.236	9.90	1.10	0.0002	10.0%
		Default	4.24	38.5%	0.094	11.00			
	2	Cyto	3.91	38.8%	0.221	10.07	1.03	0.0006	9.3%
		Default	4.57	41.1%	0.065	11.10			
Average Animal Difference:							1.17		
3T3	0.12	Cyto	2.38	24.7%	0.364	9.64	1.17	0.0012	10.8%
		Default	3.03	28.0%	0.211	10.81			
	0.25	Cyto	2.54	26.2%	0.353	9.66	1.17	0.0012	10.8%
		Default	3.21	29.6%	0.191	10.84			
	0.5	Cyto	2.87	29.4%	0.329	9.76	1.13	0.0003	10.4%
		Default	3.55	32.6%	0.157	10.90			
	1.25	Cyto	3.60	36.2%	0.267	9.95	1.03	0.0001	9.4%
		Default	4.29	39.1%	0.096	10.98			
	2	Cyto	3.96	39.1%	0.242	10.11	0.99	< .0001	8.9%
		Default	4.61	41.6%	0.067	11.10			
Average Animal Difference:							1.10		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
1	NHK	0.12	Cyto	7.23	1.043	7.25	1.75	0.1094	19.5%	
			Default	8.98	0.002	9.00				
		0.25	Cyto	7.10	1.083	7.34	1.76	0.0781	19.3%	
			Default	8.85	0.052	9.09				
		0.5	Cyto	6.90	1.116	7.62	1.76	0.0781	18.7%	
			Default	8.66	0.115	9.37				
	1.25	Cyto	6.48	1.101	8.34	1.70	0.1094	17.0%		
		Default	8.10	0.121	10.04					
	2	Cyto	6.21	1.097	8.84	1.73	0.1563	16.4%		
		Default	7.69	0.098	10.57					
	Average Animal Difference:							1.74		
	3T3	0.12	Cyto	6.18	0.881	6.20	2.80	0.0156	31.1%	
			Default	8.97	0.001	9.00				
			0.25	Cyto	6.05	0.880	6.28	2.80	0.0156	30.8%
				Default	8.85	0.047	9.09			
			0.5	Cyto	5.89	0.866	6.60	2.75	0.0156	29.5%
				Default	8.65	0.111	9.35			
		1.25	Cyto	5.54	0.875	7.28	2.74	0.0156	27.4%	
Default			8.10	0.114	10.02					
2		Cyto	5.34	0.888	7.76	2.83	0.0156	26.7%		
		Default	7.69	0.092	10.59					
Average Animal Difference:							2.79			
2		NHK	0.12	Cyto	2.94	0.176	9.35	2.79	0.0625	23.0%
	Default			5.82	0.085	12.14				
	0.25		Cyto	2.92	0.277	9.62	2.55	0.0625	21.0%	
			Default	5.70	0.065	12.17				
	0.5		Cyto	3.20	0.337	9.77	2.43	0.0625	19.9%	
			Default	5.86	0.039	12.20				
	1.25	Cyto	3.78	0.362	9.07	2.94	0.0625	24.5%		
		Default	6.31	0.076	12.01					
	2	Cyto	3.84	0.371	8.56	3.30	0.0625	27.8%		
		Default	6.33	0.040	11.85					
	Average Animal Difference:							2.80		
	3T3	0.12	Cyto	4.31	1.003	10.71	1.42	0.3125	11.7%	
			Default	5.82	0.080	12.13				
			0.25	Cyto	4.24	0.957	10.92	1.24	0.3125	10.2%
				Default	5.68	0.063	12.16			
			0.5	Cyto	4.57	0.935	11.12	1.10	0.4375	9.0%
				Default	5.89	0.052	12.22			
		1.25	Cyto	5.17	0.996	10.67	1.33	0.4375	11.1%	
Default			6.30	0.055	11.99					
2		Cyto	5.18	1.077	10.26	1.62	0.1875	13.7%		
		Default	6.33	0.046	11.88					
Average Animal Difference:							1.34			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
3	NHK	0.12	Cyto	3.04	0.779	9.97	-0.23	> .9999	-2.4%	
			Default	3.55	0.490	9.74				
		0.25	Cyto	3.04	0.531	9.98	0.16	> .9999	1.6%	
			Default	3.73	0.494	10.15				
		0.5	Cyto	3.27	0.356	10.32	0.43	> .9999	4.0%	
			Default	4.13	0.388	10.75				
	1.25	Cyto	3.80	0.252	10.46	1.17	0.0625	10.0%		
		Default	4.95	0.166	11.63					
	2	Cyto	4.07	0.377	10.14	1.62	0.0313	13.8%		
		Default	5.34	0.065	11.75					
	Average Animal Difference:							0.63		
	3T3	0.12	Cyto	3.05	0.158	9.39	0.32	> .9999	3.3%	
			Default	3.54	0.477	9.72				
		0.25	Cyto	3.06	0.139	9.62	0.51	0.8438	5.1%	
Default			3.73	0.476	10.14					
0.5		Cyto	3.25	0.078	10.01	0.69	0.3125	6.5%		
		Default	4.15	0.373	10.70					
1.25		Cyto	3.85	0.237	10.39	1.25	0.0313	10.8%		
		Default	4.98	0.165	11.64					
2	Cyto	4.19	0.299	10.28	1.48	0.0313	12.6%			
	Default	5.35	0.067	11.75						
Average Animal Difference:							0.85			
4	NHK	0.12	Cyto	3.03	0.125	9.28	-0.06	0.6875	-0.7%	
			Default	3.04	0.125	9.21				
		0.25	Cyto	3.03	0.137	9.47	-0.05	0.2969	-0.6%	
			Default	3.02	0.136	9.42				
		0.5	Cyto	3.13	0.082	9.81	-0.02	0.9375	-0.2%	
			Default	3.13	0.082	9.79				
	1.25	Cyto	3.66	0.061	10.58	-0.01	0.5781	-0.1%		
		Default	3.66	0.071	10.57					
	2	Cyto	4.11	0.068	11.10	-0.04	0.2188	-0.4%		
		Default	4.10	0.073	11.05					
	Average Animal Difference:							-0.04		
	3T3	0.12	Cyto	3.03	0.270	9.67	-0.47	0.0625	-5.1%	
			Default	3.03	0.114	9.20				
		0.25	Cyto	3.03	0.247	9.79	-0.38	0.0156	-4.0%	
Default			3.03	0.129	9.41					
0.5		Cyto	3.16	0.144	10.04	-0.24	0.5781	-2.5%		
		Default	3.13	0.084	9.79					
1.25		Cyto	3.64	0.096	10.69	-0.13	0.0313	-1.3%		
		Default	3.64	0.073	10.55					
2	Cyto	4.05	0.059	11.04	0.03	0.6875	0.2%			
	Default	4.10	0.093	11.06						
Average Animal Difference:							-0.24			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
5	NHK	0.12	Cyto	0.47	0.507	11.17	0.73	0.0977	6.2%	
			Default	0.47	0.042	11.90				
		0.25	Cyto	1.18	0.380	11.05	0.54	0.4522	4.7%	
			Default	1.18	0.092	11.59				
		0.5	Cyto	1.86	0.269	10.81	0.38	0.0166	3.4%	
			Default	1.85	0.088	11.19				
			Average Animal Difference:					0.38		
	3T3	0.12	Cyto	0.47	0.198	11.55	0.35	0.0488	2.9%	
			Default	0.46	0.044	11.90				
		0.25	Cyto	1.18	0.170	11.32	0.27	0.0674	2.3%	
			Default	1.18	0.095	11.59				
		0.5	Cyto	1.85	0.128	11.02	0.16	0.1231	1.4%	
			Default	1.86	0.079	11.18				
			Average Animal Difference:					0.17		
	6	NHK	0.12	Cyto	0.00	0.899	9.52	2.48	0.0547	20.6%
				Default	0.00	0.000	12.00			
			0.25	Cyto	0.05	0.894	9.51	2.49	0.0547	20.8%
				Default	0.04	0.000	12.00			
0.5			Cyto	0.56	0.851	9.58	2.34	0.0322	19.7%	
			Default	0.57	0.019	11.92				
			Average Animal Difference:					1.93		
3T3		0.12	Cyto	0.00	0.966	9.54	2.46	0.0273	20.5%	
			Default	0.00	0.000	12.00				
		0.25	Cyto	0.05	0.961	9.52	2.48	0.0273	20.7%	
			Default	0.05	0.001	12.00				
		0.5	Cyto	0.59	0.910	9.58	2.32	0.0195	19.5%	
			Default	0.61	0.026	11.90				
			Average Animal Difference:					1.91		

Notes:

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.

Numbers are numbers of animals unless otherwise specified

Sigma - reciprocal of slope

Cyto= using NRU-determined starting dose

Default - using default starting dose of 175 mg/kg

Appendix N-5

ATC Results for the RC Rat-Only Weight Regression – 2000 mg/kg Upper Limit

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**ATC Results for the RC Rat-Only Weight Regression
2000 mg/kg Upper Limit
Results for 46 chemicals for the 3T3 NRU and 47 chemicals for the NHK NRU
(see notes to Table 6-5 for chemicals excluded).**

Summary of Animals Used and Deaths by Cell Type

Cell Type	Sigma	Method	No. Animals Dead	% Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings
NHK	0.12	Cyto	2.30	24.9%	0.342	9.22	1.62	0.0002	14.9%
		Default	2.97	27.4%	0.208	10.84			
	0.25	Cyto	2.45	26.3%	0.325	9.29	1.58	0.0009	14.5%
		Default	3.14	28.9%	0.189	10.87			
	0.5	Cyto	2.78	29.4%	0.297	9.45	1.49	< .0001	13.6%
		Default	3.47	31.8%	0.155	10.93			
	1.25	Cyto	3.52	36.2%	0.229	9.74	1.26	< .0001	11.5%
		Default	4.24	38.5%	0.094	11.00			
	2	Cyto	3.89	39.0%	0.212	9.97	1.13	< .0001	10.2%
		Default	4.57	41.1%	0.065	11.10			
Average Animal Difference:							1.42		
ST3	0.12	Cyto	2.33	26.3%	0.361	8.84	1.97	< .0001	18.2%
		Default	3.03	28.0%	0.211	10.81			
	0.25	Cyto	2.49	27.7%	0.343	8.98	1.86	< .0001	17.1%
		Default	3.21	29.6%	0.191	10.84			
	0.5	Cyto	2.82	30.6%	0.314	9.21	1.68	< .0001	15.5%
		Default	3.55	32.6%	0.157	10.90			
	1.25	Cyto	3.56	36.9%	0.247	9.65	1.33	< .0001	12.1%
		Default	4.29	39.1%	0.096	10.98			
	2	Cyto	3.96	39.8%	0.219	9.97	1.13	< .0001	10.2%
		Default	4.61	41.6%	0.067	11.10			
Average Animal Difference:							1.59		

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
1	NHK	0.12	Cyto	6.94	0.807	6.97	2.03	0.0313	22.6%	
			Default	8.98	0.002	9.00				
		0.25	Cyto	6.82	0.845	7.06	2.04	0.0469	22.4%	
			Default	8.85	0.052	9.09				
		0.5	Cyto	6.61	0.880	7.32	2.05	0.0313	21.9%	
			Default	8.66	0.115	9.37				
		1.25	Cyto	6.19	0.854	8.02	2.02	0.0313	20.1%	
			Default	8.10	0.121	10.04				
	2	Cyto	5.92	0.873	8.54	2.04	0.2188	19.3%		
		Default	7.69	0.098	10.57					
	Average Animal Difference:							2.04		
	3T3	0.12	Cyto	6.41	0.853	6.43	2.57	0.0156	28.5%	
			Default	8.97	0.001	9.00				
		0.25	Cyto	6.29	0.849	6.52	2.56	0.0156	28.2%	
			Default	8.85	0.047	9.09				
		0.5	Cyto	6.11	0.840	6.83	2.52	0.0156	27.0%	
			Default	8.65	0.111	9.35				
		1.25	Cyto	5.75	0.847	7.52	2.50	0.0156	24.9%	
			Default	8.10	0.114	10.02				
	2	Cyto	5.53	0.855	7.99	2.60	0.0156	24.5%		
	Default	7.69	0.092	10.59						
Average Animal Difference:							2.55			
2	NHK	0.12	Cyto	2.96	0.172	9.35	2.79	0.0625	23.0%	
			Default	5.82	0.085	12.14				
		0.25	Cyto	2.91	0.247	9.55	2.62	0.0625	21.5%	
			Default	5.70	0.065	12.17				
		0.5	Cyto	3.23	0.303	9.72	2.48	0.0625	20.3%	
			Default	5.86	0.039	12.20				
		1.25	Cyto	3.81	0.365	9.02	2.98	0.0625	24.9%	
			Default	6.31	0.076	12.01				
	2	Cyto	3.87	0.411	8.55	3.30	0.0625	27.9%		
		Default	6.33	0.040	11.85					
	Average Animal Difference:							2.83		
	3T3	0.12	Cyto	3.53	0.542	9.94	2.20	0.1250	18.1%	
			Default	5.82	0.080	12.13				
		0.25	Cyto	3.50	0.525	10.14	2.02	0.1250	16.6%	
			Default	5.68	0.063	12.16				
		0.5	Cyto	3.84	0.521	10.33	1.88	0.0625	15.4%	
			Default	5.89	0.052	12.22				
		1.25	Cyto	4.53	0.490	9.91	2.08	0.0625	17.3%	
			Default	6.30	0.055	11.99				
	2	Cyto	4.65	0.583	9.64	2.24	0.0625	18.8%		
	Default	6.33	0.046	11.88						
Average Animal Difference:							2.08			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
3	NHK	0.12	Cyto	3.05	0.778	9.97	-0.23	> .9999	-2.4%	
			Default	3.55	0.490	9.74				
		0.25	Cyto	3.02	0.530	9.98	0.17	> .9999	1.7%	
			Default	3.73	0.494	10.15				
		0.5	Cyto	3.29	0.335	10.30	0.45	> .9999	4.2%	
			Default	4.13	0.388	10.75				
		1.25	Cyto	3.93	0.293	10.56	1.08	0.0938	9.2%	
			Default	4.95	0.166	11.63				
	2	Cyto	4.25	0.455	10.35	1.41	0.0313	12.0%		
		Default	5.34	0.065	11.75					
	Average Animal Difference:							0.57		
	3T3	0.12	Cyto	3.03	0.119	9.23	0.48	0.6875	5.0%	
			Default	3.54	0.477	9.72				
		0.25	Cyto	3.05	0.129	9.48	0.65	0.4375	6.4%	
			Default	3.73	0.476	10.14				
		0.5	Cyto	3.30	0.102	9.94	0.76	0.4375	7.1%	
			Default	4.15	0.373	10.70				
		1.25	Cyto	3.99	0.324	10.48	1.16	0.0313	10.0%	
			Default	4.98	0.165	11.64				
	2	Cyto	4.37	0.381	10.51	1.24	0.0313	10.6%		
	Default	5.35	0.067	11.75						
Average Animal Difference:							0.86			
4	NHK	0.12	Cyto	3.02	0.105	9.20	0.02	> .9999	0.2%	
			Default	3.04	0.125	9.21				
		0.25	Cyto	3.03	0.129	9.42	0.00	0.9375	0.0%	
			Default	3.02	0.136	9.42				
		0.5	Cyto	3.14	0.080	9.76	0.03	0.2188	0.3%	
			Default	3.13	0.082	9.79				
		1.25	Cyto	3.66	0.069	10.56	0.00	0.6875	0.0%	
			Default	3.66	0.071	10.57				
	2	Cyto	4.11	0.076	11.07	-0.02	0.4688	-0.1%		
		Default	4.10	0.073	11.05					
	Average Animal Difference:							0.01		
	3T3	0.12	Cyto	3.03	0.549	9.83	-0.63	0.3125	-6.8%	
			Default	3.03	0.114	9.20				
		0.25	Cyto	3.02	0.435	9.90	-0.49	0.4688	-5.2%	
			Default	3.03	0.129	9.41				
		0.5	Cyto	3.14	0.287	10.11	-0.32	0.8125	-3.3%	
			Default	3.13	0.084	9.79				
		1.25	Cyto	3.62	0.143	10.68	-0.13	0.3125	-1.2%	
			Default	3.64	0.073	10.55				
	2	Cyto	4.05	0.078	11.06	0.00	0.6875	0.0%		
	Default	4.10	0.093	11.06						
Average Animal Difference:							-0.31			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
5	NHK	0.12	Cyto	0.46	0.690	10.55	1.35	0.1016	11.3%	
			Default	0.47	0.042	11.90				
		0.25	Cyto	1.17	0.572	10.53	1.06	0.4131	9.2%	
			Default	1.18	0.092	11.59				
		0.5	Cyto	1.85	0.403	10.45	0.73	0.0674	6.6%	
			Default	1.85	0.088	11.19				
		1.25	Cyto	2.90	0.196	10.41	0.36	0.0264	3.4%	
			Default	2.89	0.038	10.77				
	2	Cyto	3.41	0.089	10.68	0.16	0.2061	1.5%		
		Default	3.37	0.019	10.84					
	Average Animal Difference:							0.73		
	3T3	0.12	Cyto	0.46	0.817	9.34	2.56	0.0195	21.5%	
			Default	0.46	0.044	11.90				
		0.25	Cyto	1.18	0.661	9.59	2.00	0.0488	17.2%	
			Default	1.18	0.095	11.59				
		0.5	Cyto	1.84	0.470	9.79	1.39	0.0244	12.4%	
			Default	1.86	0.079	11.18				
		1.25	Cyto	2.89	0.228	10.10	0.65	0.0674	6.0%	
			Default	2.90	0.041	10.75				
	2	Cyto	3.47	0.100	10.55	0.28	0.0127	2.6%		
	Default	3.36	0.014	10.83						
Average Animal Difference:							1.38			
6	NHK	0.12	Cyto	0.00	0.927	8.88	3.12	0.0234	26.0%	
			Default	0.00	0.000	12.00				
		0.25	Cyto	0.05	0.929	8.90	3.10	0.0244	25.9%	
			Default	0.04	0.000	12.00				
		0.5	Cyto	0.56	0.878	9.00	2.92	0.0244	24.5%	
			Default	0.57	0.019	11.92				
		1.25	Cyto	2.01	0.571	9.52	1.80	0.0244	15.9%	
			Default	2.17	0.048	11.32				
	2	Cyto	2.75	0.366	9.91	1.12	0.0244	10.2%		
		Default	2.86	0.023	11.04					
	Average Animal Difference:							2.41		
	3T3	0.12	Cyto	0.00	0.990	8.50	3.50	0.0195	29.2%	
			Default	0.00	0.000	12.00				
		0.25	Cyto	0.05	0.994	8.50	3.50	0.0195	29.1%	
			Default	0.05	0.001	12.00				
		0.5	Cyto	0.58	0.938	8.62	3.28	0.0195	27.5%	
			Default	0.61	0.026	11.90				
		1.25	Cyto	2.00	0.616	9.30	1.99	0.0273	17.7%	
			Default	2.19	0.048	11.29				
	2	Cyto	2.77	0.393	9.80	1.19	0.0371	10.9%		
	Default	2.90	0.026	10.99						
Average Animal Difference:							2.69			

Notes:

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at $p < 0.05$.

Numbers are numbers of animals unless otherwise specified

Sigma - reciprocal of slope

Cyto= using NRU-determined starting dose

Default - using default starting dose of 175 mg/kg

Appendix N-6

**ATC Results for the RC Rat-Only Weight Regression Excluding
Chemicals with Specific Mechanisms of Action – 2000 mg/kg
Upper Limit**

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**ATC Results for the RC Rat-Only Weight Regression Excluding Chemicals with Specific Mechanisms of Action
2000 mg/kg Upper Limit
46 Chemicals for the 3T3 NRU; 47 Chemicals for the NHK NRU**

Summary of Animals Used by Cell Type

Cell Type	Sigma	Method	No. Animals Dead	% Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings
NHK	0.12	Cyto	2.43	27.3%	0.305	8.91	1.94	< .0001	17.9%
		Default	2.97	27.4%	0.208	10.84			
	0.25	Cyto	2.58	28.6%	0.286	9.03	1.84	< .0001	16.9%
		Default	3.14	28.9%	0.189	10.87			
	0.5	Cyto	2.91	31.5%	0.260	9.25	1.68	< .0001	15.4%
		Default	3.47	31.8%	0.155	10.93			
	1.25	Cyto	3.65	37.6%	0.194	9.70	1.30	< .0001	11.8%
		Default	4.24	38.5%	0.094	11.00			
	2	Cyto	4.02	40.2%	0.175	10.02	1.08	< .0001	9.8%
		Default	4.57	41.1%	0.065	11.10			
Average Animal Difference:							1.57		
3T3	0.12	Cyto	2.42	28.3%	0.327	8.53	2.28	< .0001	21.1%
		Default	3.03	28.0%	0.211	10.81			
	0.25	Cyto	2.58	29.6%	0.315	8.71	2.12	< .0001	19.6%
		Default	3.21	29.6%	0.191	10.84			
	0.5	Cyto	2.92	32.4%	0.288	9.00	1.90	< .0001	17.4%
		Default	3.55	32.6%	0.157	10.90			
	1.25	Cyto	3.66	38.2%	0.227	9.60	1.38	< .0001	12.5%
		Default	4.29	39.1%	0.096	10.98			
	2	Cyto	4.06	40.6%	0.207	10.00	1.10	< .0001	9.9%
		Default	4.61	41.6%	0.067	11.10			
Average Animal Difference:							1.76		

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. Boldfaced values are significant values at $p < 0.05$.

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
1	NHK	0.12	Cyto	7.73	0.578	7.76	1.24	0.0938	13.8%	
			Default	8.98	0.002	9.00				
		0.25	Cyto	7.61	0.608	7.84	1.25	0.0781	13.8%	
			Default	8.85	0.052	9.09				
		0.5	Cyto	7.40	0.651	8.11	1.27	0.0313	13.5%	
			Default	8.66	0.115	9.37				
		1.25	Cyto	6.91	0.646	8.79	1.25	0.0156	12.5%	
			Default	8.10	0.121	10.04				
	2	Cyto	6.59	0.654	9.32	1.26	0.2188	11.9%		
		Default	7.69	0.098	10.57					
	Average Animal Difference:							1.25		
	3T3	0.12	Cyto	6.81	0.856	6.84	2.16	0.0156	24.0%	
			Default	8.97	0.001	9.00				
		0.25	Cyto	6.69	0.838	6.93	2.16	0.0156	23.7%	
			Default	8.85	0.047	9.09				
		0.5	Cyto	6.53	0.829	7.23	2.12	0.0781	22.6%	
			Default	8.65	0.111	9.35				
		1.25	Cyto	6.13	0.830	7.93	2.09	0.1563	20.9%	
			Default	8.10	0.114	10.02				
		2	Cyto	5.87	0.863	8.40	2.19	0.0469	20.6%	
Default			7.69	0.092	10.59					
Average Animal Difference:							2.14			
2		NHK	0.12	Cyto	3.14	0.268	9.52	2.62	0.0625	21.6%
	Default			5.82	0.085	12.14				
	0.25		Cyto	3.09	0.304	9.74	2.43	0.0625	20.0%	
			Default	5.70	0.065	12.17				
	0.5		Cyto	3.39	0.331	9.87	2.33	0.0625	19.1%	
			Default	5.86	0.039	12.20				
	1.25		Cyto	4.01	0.447	9.28	2.73	0.0625	22.7%	
			Default	6.31	0.076	12.01				
	2	Cyto	4.11	0.506	8.87	2.98	0.0625	25.2%		
		Default	6.33	0.040	11.85					
	Average Animal Difference:							2.62		
	3T3	0.12	Cyto	3.79	0.537	10.18	1.96	0.1250	16.1%	
			Default	5.82	0.080	12.13				
		0.25	Cyto	3.77	0.519	10.40	1.76	0.1250	14.5%	
			Default	5.68	0.063	12.16				
		0.5	Cyto	4.07	0.502	10.52	1.70	0.1250	13.9%	
			Default	5.89	0.052	12.22				
		1.25	Cyto	4.75	0.519	10.14	1.86	0.1250	15.5%	
			Default	6.30	0.055	11.99				
		2	Cyto	4.83	0.633	9.86	2.02	0.1250	17.0%	
Default			6.33	0.046	11.88					
Average Animal Difference:							1.86			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
3	NHK	0.12	Cyto	3.03	0.606	9.80	-0.06	0.8125	-0.6%	
			Default	3.55	0.490	9.74				
		0.25	Cyto	3.04	0.439	9.86	0.29	> .9999	2.8%	
			Default	3.73	0.494	10.15				
		0.5	Cyto	3.29	0.262	10.19	0.55	0.4375	5.2%	
			Default	4.13	0.388	10.75				
		1.25	Cyto	3.99	0.311	10.60	1.03	0.1563	8.8%	
			Default	4.95	0.166	11.63				
	2	Cyto	4.30	0.446	10.42	1.33	0.1563	11.3%		
		Default	5.34	0.065	11.75					
	Average Animal Difference:							0.63		
	3T3	0.12	Cyto	3.05	0.125	9.24	0.48	0.5000	4.9%	
			Default	3.54	0.477	9.72				
		0.25	Cyto	3.06	0.129	9.49	0.65	0.3125	6.4%	
			Default	3.73	0.476	10.14				
		0.5	Cyto	3.34	0.086	9.92	0.79	0.4375	7.3%	
			Default	4.15	0.373	10.70				
		1.25	Cyto	4.10	0.319	10.60	1.05	0.1563	9.0%	
			Default	4.98	0.165	11.64				
	2	Cyto	4.49	0.406	10.66	1.09	0.0625	9.3%		
Default		5.35	0.067	11.75						
Average Animal Difference:							0.81			
4	NHK	0.12	Cyto	3.03	0.118	9.21	0.01	0.7188	0.1%	
			Default	3.04	0.125	9.21				
		0.25	Cyto	3.01	0.134	9.43	-0.01	0.4688	-0.1%	
			Default	3.02	0.136	9.42				
		0.5	Cyto	3.15	0.080	9.79	0.00	0.9375	0.0%	
			Default	3.13	0.082	9.79				
		1.25	Cyto	3.67	0.073	10.58	-0.01	0.5781	-0.1%	
			Default	3.66	0.071	10.57				
	2	Cyto	4.13	0.086	11.09	-0.03	0.9375	-0.3%		
		Default	4.10	0.073	11.05					
	Average Animal Difference:							-0.01		
	3T3	0.12	Cyto	3.03	0.130	9.24	-0.03	0.5625	-0.4%	
			Default	3.03	0.114	9.20				
		0.25	Cyto	3.03	0.123	9.43	-0.02	0.5625	-0.2%	
			Default	3.03	0.129	9.41				
		0.5	Cyto	3.16	0.067	9.77	0.02	0.4688	0.2%	
			Default	3.13	0.084	9.79				
		1.25	Cyto	3.68	0.078	10.59	-0.03	0.4688	-0.3%	
			Default	3.64	0.073	10.55				
	2	Cyto	4.13	0.064	11.09	-0.03	0.6875	-0.3%		
Default		4.10	0.093	11.06						
Average Animal Difference:							-0.02			

Summary of Animals Used by GHS Toxicity Category and Cell Type

Category	Cell Type	Sigma	Method	No. Animals Dead	Std. Error (dosed)	No. Animals Dosed	Difference	P-value*	% Savings	
5	NHK	0.12	Cyto	0.46	0.795	9.62	2.28	0.0195	19.2%	
			Default	0.47	0.042	11.90				
		0.25	Cyto	1.18	0.633	9.81	1.77	0.0322	15.3%	
			Default	1.18	0.092	11.59				
		0.5	Cyto	1.84	0.448	9.96	1.23	0.0137	11.0%	
			Default	1.85	0.088	11.19				
		1.25	Cyto	2.89	0.212	10.19	0.58	0.0049	5.4%	
			Default	2.89	0.038	10.77				
	2	Cyto	3.45	0.100	10.58	0.26	0.0830	2.4%		
		Default	3.37	0.019	10.84					
	Average Animal Difference:							1.23		
	3T3	0.12	Cyto	0.46	0.822	8.83	3.07	0.0020	25.8%	
			Default	0.46	0.044	11.90				
		0.25	Cyto	1.16	0.674	9.19	2.39	0.0098	20.6%	
			Default	1.18	0.095	11.59				
		0.5	Cyto	1.83	0.472	9.50	1.67	0.0049	15.0%	
			Default	1.86	0.079	11.18				
		1.25	Cyto	2.90	0.219	9.99	0.77	0.0049	7.1%	
			Default	2.90	0.041	10.75				
	2	Cyto	3.48	0.112	10.51	0.32	0.0186	2.9%		
Default		3.36	0.014	10.83						
Average Animal Difference:							1.64			
6	NHK	0.12	Cyto	0.00	0.810	7.96	4.04	0.0078	33.7%	
			Default	0.00	0.000	12.00				
		0.25	Cyto	0.04	0.809	7.96	4.04	0.0098	33.7%	
			Default	0.04	0.000	12.00				
		0.5	Cyto	0.56	0.761	8.13	3.79	0.0029	31.8%	
			Default	0.57	0.019	11.92				
		1.25	Cyto	1.96	0.481	8.95	2.37	0.0010	20.9%	
			Default	2.17	0.048	11.32				
	2	Cyto	2.70	0.309	9.53	1.51	0.0098	13.7%		
		Default	2.86	0.023	11.04					
	Average Animal Difference:							3.15		
	3T3	0.12	Cyto	0.00	0.819	7.62	4.38	0.0078	36.5%	
			Default	0.00	0.000	12.00				
		0.25	Cyto	0.05	0.823	7.63	4.37	0.0098	36.4%	
			Default	0.05	0.001	12.00				
		0.5	Cyto	0.58	0.773	7.82	4.08	0.0098	34.3%	
			Default	0.61	0.026	11.90				
		1.25	Cyto	1.96	0.497	8.80	2.49	0.0059	22.1%	
			Default	2.19	0.048	11.29				
	2	Cyto	2.74	0.311	9.47	1.52	0.0098	13.8%		
Default		2.90	0.026	10.99						
Average Animal Difference:							3.37			

*P-Value is from one-side Wilcoxon Signed Ranked test for difference in animal use between the default and cytotoxicity methods. **Boldfaced** values are significant values at p < 0.05.